I. Remarks

Claims herein under examination are claims 1-6.

II. Claim rejections under 35 U.S.C. § 103(a)

Claims 1-6 stand rejected under 35 U.S.C. 103(a) as being allegedly unpatentable over Diebold *et al.*, 1999, *J. Biol. Chem.* 247:19087-19094 ("Diebold") in view of Scheicher *et al.*, 1995, *Eur. J. Immunol.* 25:1566-1572 ("Scheicher").

Specifically, the Office alleges that it would have been obvious to incorporate microbeads into Diebold's Ad/Man/PEI complexes. The Office alleges that one would have been motivated by Scheicher's teaching that bead-adsorbed antigen carriers targeted to dendritic cells result in much more efficient antigen presentation than soluble antigen, as allegedly used by Diebold. The Office further alleges that one would have had a reasonable expectation of success that the bead-adsorbed system of Scheicher would work with Diebold's Ad/ManPEI/DNA complexes because mannose receptors are expressed in high levels on dendritic cells and because the complexes were able to target dendritic cells and display the antigenic peptide. Applicant respectfully traverses.

Claims 1-6 are not obvious in view of the prior art cited by the Office. The establishment of a *prima facie* case of obviousness requires, in part, a suggestion or motivation to modify the prior art references. (MPEP 2143). If these proposed modifications render the prior art invention unsatisfactory for its intended purpose, there is no suggestion or motivation to make the proposed modification (MPEP 2143.01). Also, if the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims prima facie obvious (MPEP 2143.01). Applicants assert that the prior art modifications proposed by the Office renders the prior art 1) unsatisfactory for its intended purpose and 2) changes the principle of operation of the prior art. Therefore, no prima facie case of obviousness has been established or can be established based on a combination of the prior art cited by the Office.

The Office suggests that it would have been obvious to incorporate microbeads into the Diebold Ad/ManPEI/DNA composition. However, Applicant notes that the incorporation of the large, polystyrene particle (1 micron) provided by Scheicher is a modification that would render the Diebold composition unsatisfactory for its intended purpose. Such a modification would also change the principles of operation of the Diebold composition.

The Diebold reference teaches the formation of mannosylpolyethylenimine (ManPEI), DNA, and adenoviral particle complexes (Ad/ManPEI/DNA) for gene delivery purposes via receptor mediated endocytosis (see Diebold at Abstract, page 19087; at page 19088, lines 3-6; at page 19089, col. 1, 2^{cd} full paragraph). Diebold incorporated adenoviral particles (wild-type adenovirus, E4 negative Ad5 adenovirus, or psoralen-inactivated E4 negative Ad5 adenovirus) into the ManPEI/DNA composition in order to increase its efficacy (see Diebold at page 19090, col. 1, line 37 - col. 2, line 3). Diebold teaches that the adenovirus particles provide one of two functions: 1) they act as an endosomolytic agent to release DNA from the endosomal compartment following receptor mediated endocytosis or 2) they increase the uptake of the composition via the adenoviral internalization route (see Diebold at page 19092, col. 1, line 13 - col. 2, line 18). Under either proposed mechanism, Diebold teaches that the Ad/ManPEI/DNA undergoes receptor-mediated endocytosis whether by the mannose receptor or by the adenoviral receptor.

The Scheicher reference teaches that a certain subset of dendritic cells were capable of phagocytosis, as measured by their ability to take up 1 micron, polystyrene beads (see Scheicher at page 1566, Abstract, lines 9-15; page 1567, col. 1, lines 10-21; page 1568, Results, 1st paragraph). Capitalizing on the phagocytic ability of these dendritic cell precursors, Scheicher delivers antigen to the cells using polystyrene beads to which the antigen has been adsorbed. Scheicher distinguishes this phagocytic route of bead entry from that of either pinocytosis or endocytosis, which is a distinction appreciation by one of ordinary skill in the art (see Scheicher at page 1567, col. 1, lines 7-21, at page 1570, Figure 4; page 1571, col. 2, lines 32-42).

Following the Scheicher teachings, the incorporation of the polystyrene bead would thus target the Ad/ManPEI/DNA composition to a phagocytic entry route rather than to the endocytic route targeted by the unmodified composition. The addition of the polystyrene beads to the Diebold Ad/ManPEI/DNA composition would render it unsatisfactory for its intended purpose, which is to deliver DNA via receptor mediated endocytosis. Moreover, by altering the entry route of the Ad/ManPEI/DNA composition, the Office's modification impermissibly alters the principles of operation of the Diebold composition from that of endocytic entry to that of phagocytic entry.

Since the prior art modifications proposed by the Office render the prior art 1) unsatisfactory for its intended purpose and 2) change the principle of operation of the prior art, no prima facie case of obviousness has been established or can be established based on a combination of the prior art cited by the Office. Applicant respectfully requests withdrawal of this rejection and that the claims be allowed to proceed to issuance.

III. In the claims:

1. (Original) An adenovirus particulate comprising a plurality of adenovirus particles complexed to an insoluble micro-platform material.

2. (Original) The adenovirus particulate of claim 1 further comprising a cell binding ligand complexed to the micro-platform material.

3. (Original) The adenovirus particulate of claim 2 wherein the cell binding ligand binds to a receptor on a dendritic cell.

4. (Original) The adenovirus particulate of claim 3 wherein the cell binding ligand is selected from the group consisting of GM-CSF, mannose, and mannose-6-phosphate.

5. (Original) The adenovirus particulate of claim 1 wherein the micro-platform material is a polymeric fiber or microbead.

6. (Original) The adenovirus particulate of claim 5 wherein the adenovirus particulate further comprises a gene encoding an antigenic polypeptide.

7. (Withdrawn) A method of forming a particulate composed of adenovirus particles comprising mixing adenovirus particles with an insoluble micro-platform material so that the adenovirus particles become complexed to the micro-platform material.

8. (Withdrawn) The method of claim 7 where the micro-platform material is a polymeric fiber or microbead.

9. (Withdrawn) The method of claim 7 wherein the adenovirus particles are complexed to the microplatform material by a crosslinking agent.

10. (Withdrawn) The method of claim 8 wherein the adenovirus particles are complexed to the microplatform material by a crosslinking agent.

11. (Withdrawn) The method of claim 9 where the cross-linking substance is a bivalent antibody.

12. (Withdrawn) The method of claim 10 where the cross-linking substance is a bivalent antibody.

13. (Withdrawn) A method of forming a particulate of adenovirus particles where the adenovirus particle further comprises a gene encoding an antigenic polypeptide.

14. (Withdrawn) The method of claim 7 wherein the particulate of adenovirus particles further comprises a ligand that binds to a receptor on a dendritic cell.

15. (Withdrawn) The method of claim 14 wherein the ligand is GM-CSF, mannose, or mannosed phosphate.

16. (Withdrawn) The method of claim 13 wherein the particulate of adenovirus particles further comprises a ligand that binds to a receptor on a dendritic cell.

17. (Withdrawn) The method of claim 16 wherein the ligand is GM-CSF, mannose, or mannose-6-phosphate.

18. (Withdrawn) A method of transfecting a dendritic cell comprising contacting a dendritic cell with an adenovirus particulate of claim 1, thereby transfecting the cell.

19. (Withdrawn) A method of vaccinating a subject against a disease comprising administering to the subject an adenovirus particulate of claim 6, thereby vaccinating the subject against a disease.

20. (Withdrawn) A method of claim 19 where the adenovirus particulate vaccine is administered together with an adjuvant.

IV. Conclusion

No fee is deemed necessary in connection with the filing of this communication. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 07-1074.

Respectfully submitted,

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Date

Jennifer D. Tousignant
Agent for Applicants
Registration No. 54,498
Telephone: (508) 270-2499
Facsimile: (508) 872-5415

GENZYME CORPORATION
15 Pleasant Street Connector
P.O. Box 9322
Framingham, Massachusetts 01701-9322